

Trends in hospital morbidity from Alzheimer's disease in the European Union, 2000-2014

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Abstract

Background: Alzheimer's disease (AD) has become a concerning public health issue. We aimed to analyse the trends of hospital morbidity from AD in the European Union (EU) in the period 2000-2014. **Methods:** Data from hospital discharges of men and women over 50 years old hospitalised from AD in the EU were extracted from Eurostat database. We tested for secular trends computing the annual percent change, and identifying significant changes in the linear slope of the trend. **Results:** Hospital morbidity from AD showed a 0.8% (95% confidence intervals -2.2, 0.6) slight declining trend in the EU. In men and women, we recorded a -0.5% and -1.0% decrease in hospital morbidity rates, respectively. Several countries showed changing trends during the study period. **Conclusion:** AD hospital morbidity has slightly declined in the entire EU in the past years. Eastern European countries showed steadily increasing trends, whereas in western and Mediterranean countries rates decreased or levelled off.

Keywords: Alzheimer's disease; Hospital morbidity; Trends; European Union; Joinpoint analysis

Introduction

Alzheimer's disease (AD) is the most common type of dementia, accounting for 60-70% of all cases.¹ In 2015, almost 47 million people worldwide suffered from dementia, and this figure could reach 131 million by 2050. Among them, the number of patients in Europe is estimated to rise from 10.46 million in 2015 to almost 19 million in 2050.²

Several studies have studied the epidemiology of AD in different world regions. In European countries, a meta-analysis estimated that the overall prevalence and incidence in people older than 55 years were 5.05%, and 11.08 per 1000 person-years, respectively,³ and mortality has increased in the past decades.⁴ In the United States, prevalence of the disease was 9.51%,⁵ while in developing countries was estimated to be 3.4%.⁶

Patients with AD live several years from the onset of the disease,⁷ and are at higher risk for hospitalisation.⁸ Therefore, AD lead to a great societal and economic burden. In Europe, in 2010 the total costs of dementia reached 238 billion dollars, of which direct medical costs accounted for 36 billion dollars,⁹ whilst total payments for health care, long-term care and hospice for patients with AD and other dementias in the United States were estimated at 236 billion dollars.¹⁰

Despite the well-known impact of AD, to date, there is a lack of research regarding the trends of hospital morbidity from the disease, probably given its role of underlying, but not main condition, for hospitalisation in many cases. Therefore, we aimed to analyse the trends of hospital morbidity from AD in the European Union (EU) in the period 2000-2014. Our findings may reflect the trajectories of hospitalisations from the disease in European countries in the past years, thus providing new evidence essential for planning public health policies.

Methods

Data from hospital discharges, defined as formal release of a patient from a hospital, including patients discharged alive, dead or transferred to another hospital,¹¹ of men and women over 50 years old hospitalised from AD (defined as the main condition determined

as principal cause of the episode of hospitalisation) for a minimum of one night or more than 24 hours (in-patient) or discharged on the same day (day-cases) in the member countries of the EU. We extracted data from Eurostat, the statistical office of the EU, for the period 2000-2014 due to the availability of the data for most of European countries in these years.¹² Eurostat receives data from each country's statistical authorities, checks the comparability of the data and ensures the internal coherence by annual validation processes.

Diagnosis for hospital discharges were coded using the International Shortlist for Hospital Morbidity Tabulation (ISHMT).¹³ Code 0601 (Alzheimer's disease, International Classification of Diseases (ICD) 9th and 10th revision codes 331.0 and G30, respectively) was used.

To broaden the focus of the study, we conducted an additional analysis of men and women over 50 years old hospitalised from dementia. Diagnosis for hospital discharges were coded with ICD codes F00-F03.¹²

Estimates of resident population, based on official censuses, were also extracted from the Eurostat database.¹⁴

The EU member countries and their data availability included: Austria (2000-2014), Belgium (2000-2009, 2011-2013), Croatia (2002-2014), Cyprus (2005-2007, 2010-2013), Czech Republic (2000-2014), Denmark (2000-2014), Finland (2001-2014), France (2000-2014), Germany (2000-2014), Hungary (2004-2014), Ireland (2000-2014), Italy (2001-2014), Latvia (2004-2014), Lithuania (2001-2014), Luxembourg (2002-2014), the Netherlands (2004-2012), Poland (2005-2014), Portugal (2000-2014), Slovakia (2000-2012, 2014), Slovenia (2004-2014), Spain (2000-2014), and the United Kingdom (2000-2014).

Unfortunately, for several countries (Bulgaria, Greece, Estonia, Malta, Romania and Sweden) most of the data were not available, and were excluded from the study. In addition, in a few countries data for one or more calendar years were missing. No

extrapolation was made for missing data, assuming trends would not vary substantially in countries with less missing data, whereas in countries with more missing data, results should be interpreted carefully.

From the number of hospitalisations and resident population, age-standardised hospital morbidity rates per 100,000 for each 5-year age group (from 50-54 to 85 and older) and calendar period for men and women were computed, using the direct method and based on the 2013 European Standard Population. Some countries (Czech Republic, Denmark, Italy and Slovenia, these two latter countries only for day-cases) considered multi-episodes cases as one hospital discharge, while the remaining countries considered them as separate discharge records, or do not allude to this issue.¹¹

Joinpoint regression software (version 4.2.0.2), provided by the Surveillance Research Program of the USA National Cancer Institute (Bethesda, MD, USA), was used to analyse significant changes in morbidity trends. This analysis identifies inflexion points (joinpoints) at which there was a significant change in the linear slope of the trend.¹⁵

We computed the estimated annual percent change (APC) and corresponding 95% confidence intervals (95% CIs), describing the magnitude of change of the identified trends. In this model, age-standardised morbidity rates were used as the dependent variable, and the year of hospital discharge as the independent variable. A p value lower than 0.05 was considered as statistically significant. No approval by an institutional review board was required.

Results

Trends of hospital morbidity from Alzheimer's disease

Between 2000 and 2014, the number of hospital discharges of in-patients and day-cases over 50 years old hospitalised by AD in the EU increased from 38,428 to 59,937.

Throughout the study period, among the member states of the EU, the highest

hospital morbidity rates were found in Finland, Belgium and Austria, whereas Cyprus, Latvia, Denmark and Portugal showed the lowest rates. The highest overall age-standardised morbidity rate was observed in Finland in 2007, 329.7 per 100,000, and in Latvia we found the lowest, 0.7 per 100,000, in the year 2006. (Supplemental Data 1)

During the 2000-2014 period, the entire EU showed a slight non-significant downward trend (APC=-0.8%; 95% CI -2.2, 0.6), identifying two joinpoints. Between 2000 and 2004, hospital morbidity rates showed a statistically significant rising trend (APC=6.6%; 95% CI 2.2, 11.1), followed by a significant decrease in the period 2004-2012 (APC=-1.8%; 95% CI -3.5, -0.1), and a non-significant pronounced downward trend thereafter (APC=-11.4%; 95% CI -22.4, 1.2).

Morbidity rates increased in 12 countries throughout the EU. The Netherlands, Latvia and Spain showed the largest growths, whereas Finland and Germany had the less pronounced increases. On the contrary, the remaining 10 countries showed overall downward trends, recording in France, Luxembourg, and Italy the steepest declines, whilst in Hungary and Portugal morbidity rates descended slightly. (Table 1)

Trends of hospital morbidity from Alzheimer's disease in men

In 2000, the highest rates in men were recorded in France, Belgium and Czech Republic (over 50 per 100,000), while Spain, Slovakia, Denmark, and Portugal showed the lowest (below 8 per 100,000). In 2014, we observed the highest rates in Finland, Czech Republic and Slovenia (over 80 per 100,000), and the lowest in Denmark, Portugal and Latvia (below 9 per 100,000). (Supplemental Data 2)

Along the study period, European men showed an overall non-significant downward trend in hospital morbidity (APC=-0.5%; 95% CI -1.8, 0.8), identifying two joinpoints. In the first years, a statistically significant growing trend was recorded, followed by non-significant decreasing trends afterwards, more pronounced in the latter years.

Morbidity rates rose in 13 countries. The Netherlands, Latvia and Spain showed the steepest increasing trends, while in Cyprus, Hungary and Finland the less pronounced

growing trends were observed. Conversely, in 9 countries rates lessened over the study period. In France, Italy and Luxembourg we recorded the largest declining trends, whilst in Portugal, Austria, Croatia and the United Kingdom we found the less pronounced decreases. (Table 2)

In Austria, Denmark, Finland, France and Poland, APC peaked, decreasing thereafter. Hospital morbidity rates in Italy increased at a lower rate in the first years, almost levelling off, significantly descending afterwards. In Germany and Spain, after a significant increasing trend in the first period, rates continued growing at a lower rate, in contrast to the Netherlands, where rose sharply in the last years. In Czech Republic and Slovakia fluctuating trends were observed.

Trends of hospital morbidity from Alzheimer's disease in women

For European women, in 2000 we found the highest rates in France, Belgium and Czech Republic (over 60 per 100,000), and the lowest in Spain, Slovakia, Portugal and Denmark (below 6 per 100,000). In 2014, the highest rates were recorded in Finland, Czech Republic and Slovenia (over 80 per 100,000), and the lowest in Denmark and Portugal (below 7 per 100,000). (Supplemental Data 3)

Likewise, among women, an overall non-significant downward trend was recorded (APC=-1.0%; 95% CI -2.4; 0.5), identifying two joinpoints. We observed a significant growing trend in the first years, followed by a significant decrease, and a more pronounced non-significant declining trend in the latter years.

During the study period, 13 countries showed an upward trend. The Netherlands, Latvia and Spain showed the steepest growths, while in Finland, Germany and Portugal rates increased slightly or almost levelled off. In contrast, 9 countries showed declining trends. France, Luxembourg and Croatia had the largest decreases, whilst Austria, Denmark and Hungary showed the less pronounced declines. (Table 3)

In Austria, Denmark, Finland, France, Germany, Italy and Poland, APCs peaked, declining thereafter. In two countries (Lithuania and Slovenia), significant pronounced

upward trends were recorded in the first period, significantly increasing at a lower rate afterwards, contrasting with the pronounced growing trend found in the Netherlands in the latter years. In Croatia and Hungary morbidity rates lowered in the first period, showing a non-significant rising in the latter. In Slovakia and Spain, fluctuating trends were observed.

Trends of hospital morbidity by gender in the whole EU are shown in Figure 1. Except in Austria, Denmark, Finland, Germany, the Netherlands, Poland, Slovakia and Spain, trends were more pronounced in women than in men. Furthermore, in Hungary and Portugal, trends were divergent. (Figure 2)

Trends of hospital morbidity from dementia

Between 2000 and 2014, hospital morbidity rates from dementia showed a significant downward trend (APC=-3.9%; 95% CI -4.2, -3.7). We did not identify any joinpoints.

Morbidity rates increased in 4 countries: Cyprus, Ireland, Latvia and Slovenia. In the first 3 countries, we recorded the largest increases (all statistically significant), especially in Cyprus. Conversely, the remaining countries showed overall declining trends. We found in Belgium, Germany, Italy and Lithuania the steepest decreases, whilst in Croatia, France and Slovakia morbidity rates declined slightly. (Supplemental Data 4-6)

Morbidity trends from AD and dementia showed the same direction in 12 countries (Austria, Croatia, Cyprus, Denmark, France, Hungary, Italy, Latvia, Luxembourg, Portugal, Slovenia and the United Kingdom), while in the remaining 10 countries (Belgium, Czech Republic, Finland, Germany, Ireland, Lithuania, the Netherlands, Poland, Slovakia and Spain) hospital morbidity trends were divergent.

Discussion

To the best of our knowledge, this is the first study analysing the trends in hospital

morbidity from AD in the EU according to hospital discharge data. Our results indicate that, despite the growing number of hospital discharges, trends declined slightly in both sexes along the past years. By countries, the steepest increases were found in the Netherlands, Latvia and Spain, whereas in France, Luxembourg and Italy we recorded the largest descending trends.

Our results are in line with a US study which reported a slight decline of trends in hospitalisations between 1999 and 2009, describing an increasing trend in the first years, followed by a subsequent decrease.¹⁶ In other European studies, both prevalence of dementia in hospitalised population and hospitalisation rates tended to increase in the early 2000s, which also seem to be consistent with our findings.^{17,18}

This study retrieved data from 22 EU countries. Therefore, differences in diagnosis and hospital practice, discharge patterns and cultural differences within these countries, considered as inherent factors, might explain to a certain extent the divergences observed. In this line, in a previously published study, Waldemar *et al.*¹⁹ identified the economic barriers, including not only differences in per capita gross domestic product, but variations in care costs across European regions,²⁰ the fear of social stigma and cultural beliefs and the lack of specialists as the main barriers affecting the access to diagnostic evaluation and treatment for the disease in EU.

In the former-Soviet Baltic States and eastern European countries, where steady growing trends were recorded, improvement of social conditions, economic development, and the adoption of healthier lifestyle habits, which have led to the rise of life expectancy in the past decades,²¹ and therefore to rising prevalence of age-related diseases such as AD, might be a reason of the trends observed. Also, changes in the survival period among people who suffer the disease, with a prolonged survival of several years,^{22,23} might increase the probability to be hospitalised for this cause.

Conversely, in most of the western and Mediterranean countries, after increasing in the first years, hospitalisation rates tended to decrease. Prior investigations have ascertained that prevalence of dementia have lessened in these countries,²⁴ probably due

to societal changes that brought about better living conditions, and the progressive adherence to healthier lifestyles.²⁵ Therefore, we speculate that the lowering in prevalence might be, to a certain extent, related to the descending trends observed in the latter years. Other related factor that may explain this decline is the considerable increase in utilization of ambulatory services and primary care services by patients diagnosed with AD,^{26,27} especially among rural population.²⁸

In some countries, very pronounced upward trends were observed in the first study period. We propose several hypotheses for this observation. On the one hand, this could be the reflection of an increase awareness of the condition by the physicians, as reported in a Finnish study finding that predictive positive value for hospital discharge diagnoses improved considerably after 1998.²⁹ On the other hand, methodological issues, e.g. in Austria, there was a change from ICD-9 to ICD-10 in year 2001¹¹ could explain the sharp increasing trend observed in this country.

The fact that, despite recent efforts, AD is still underreported in hospital discharge registers, should also be mentioned. In a Swedish study testing two disease registries, sensitivity was 55%, thus missing 45% of prevalent patients in the inpatient registry.³⁰ More recently, Douzenis *et al.*³¹ also found that cognitive decline was greatly underdiagnosed.

Other factor that may confuse AD diagnosis is the fact that some patients might suffer delirium during their hospital stay. Some investigations reported that prevalence of delirium in older patients ranged between 16% to 20%.^{32,33} Also, delirium appears to be phenomenologically similar among patients with or without dementia.³⁴ This fact may lead to misdiagnose AD among non-dementia patients and should be taken into account. We could not use algorithms to validate AD diagnosis in this study and should be acknowledged. However, Eurostat conducts annual validation processes and consistency checks,¹¹ thus we assume data used have sufficiency quality to ensure study's validity.

One of the reasons of this underreporting might be that most of the patients with AD were not admitted for the disease itself, but to co-morbid conditions.³⁵ Comorbidities,

besides being independently associated with higher costs of care,³⁶ also increased the risk of subsequent hospital admission and emergency department visit.³⁷ In this line, Browne *et al.*³⁸ found that the clear majority of patients with dementia had at least one comorbid condition, and reported that a higher number of comorbidities was related to increased primary care consultation rates and hospital admission rates. Other recent investigations also found that comorbidity burden of patients with dementia was heavier than non-dementia patients.³⁹ This fact difficult the recognition and correct diagnosis of AD by the physicians when a patient is admitted, consequently leading to underreport the real AD hospitalization. This underreport is reflected in our findings, where only those patients diagnosed with AD as the main cause of hospitalisation were included. Therefore, it seems reasonable to assume that the real hospital morbidity rate might be higher.

Another issue that deserve discussion is that many of the elderly with AD might have been admitted to nursing homes. In institutionalised persons, probability of hospitalisation decreased as dementia worsened.^{40,41} However, this institutionalised population has not been considered in this study, as well as people treated at home. Therefore, it is plausible to think that we might have underestimated the real hospital morbidity rates.

As expected, morbidity trends in women were more pronounced than in men in most of European countries, possibly due to their longer life expectancy,⁴² and biological and social factors.⁴³

Our study has several strengths. To our knowledge, this is a novel study analysing hospital morbidity trends in the whole of the EU. In addition, we decided to only use official data, and not extrapolate or impute any missing data, which ensure the validity of our results. However, this work also has some limitations. First, the lack of data from several years or the whole period in some countries, whose inclusion would have improved the validity and generalization of our results. Second, the use of ICD codes may influence diagnosis coding, leading to under-code the condition.⁴⁴ This fact affects to some extent the validity of our data and should be taken into account. Another limitation

is the non-inclusion of institutionalised population, which could have led to underreport the real morbidity, and should be duly acknowledged.

In summary, our findings confirmed a slight downward trend of hospital morbidity from AD in the EU, according to hospital discharge data, in the past years. Disparities among countries were observed, finding steady growing trends mainly in eastern European countries, whereas in most of western and Mediterranean countries hospital morbidity rates tended to decrease or almost levelled off, especially in the latter years. This novel approach in studying trajectories of hospitalisation from AD in the European Union provide new evidence for planning future public health policies in aged societies. The inclusion of institutionalised population, the effect of medical awareness and diagnostic improvements, and inclusion of secondary hospital diagnoses, deserve further studies.

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Table 1. Joinpoint analysis for Alzheimer's disease hospital morbidity trends in the European Union, 2000-2014.

	Total study period		Period 1		Period 2		Period 3	
	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)
European Union	2000-2014	-0.8 (-2.2, 0.6)	2000-2004	6.6* (2.2, 11.1)	2004-2012	-1.8* (-3.5 -0.1)	2012-2014	-11.4 (-22.4, 1.2)
Austria	2000-2014	-1.4 (-6.8, 4.3)	2000-2002	104.8* (17.6, 256.8)	2002-2014	-6.8* (-9.8, -3.7)	-	-
Belgium	2000-2013	10.4* (7.9, 12.9)	-	-	-	-	-	-
Croatia	2002-2014	-4.5* (-7.6, -1.2)	2002-2012	-7.0* (-11.0, -2.9)	2012-2014	24.3 (-28.6, 116.6)	-	-
Cyprus	2005-2013	9.1 (-1.6, 21.0)	-	-	-	-	-	-
Czech Republic	2000-2014	4.4* (3.7, 5.2)	-	-	-	-	-	-
Denmark	2000-2014	-2.1 (-5.0, 0.9)	2000-2006	5.7* (1.6, 10.1)	2006-2012	-3.2 (-8.2, 2.1)	2012-2014	-30.4* (-45.2, -11.7)
Finland	2001-2014	2.7* (1.4, 4.0)	2001-2007	7.5* (5.9, 9.2)	2007-2011	-2.2 (-6.6, 2.4)	2011-2014	2.2 (-2.4, 7.0)
France	2000-2014	-7.0* (-10.2, -3.7)	2000-2007	3.4 (-1.7, 8.7)	2007-2014	-16.4* (-20.5, -12.1)	-	-
Germany	2000-2014	3.1* (1.5, 4.7)	2000-2003	16.7* (11.3, 22.4)	2003-2007	3.1 (-1.7, 8.1)	2007-2014	-0.3 (-1.6, 0.9)
Hungary	2004-2014	-0.2 (-4.5, 4.4)	2004-2008	-11.9 (-23.5, 1.6)	2008-2014	7.2 (-0.7, 15.6)	-	-
Ireland	2000-2014	-3.4* (-5.0, -1.7)	-	-	-	-	-	-
Italy	2001-2014	-5.0* (-6.8, -3.1)	2001-2005	1.4 (-1.1, 3.8)	2005-2009	-2.6 (-6.3, 1.2)	2009-2014	-11.9* (-13.4, -10.4)
Latvia	2004-2014	18.7* (4.4, 34.9)	-	-	-	-	-	-
Lithuania	2001-2014	9.8* (7.1, 12.6)	2001-2004	28.3* (13.0, 45.7)	2004-2014	6.8* (4.7, 8.9)	-	-
Luxembourg	2002-2014	-5.3* (-7.3, -3.2)	-	-	-	-	-	-
Netherlands	2004-2012	27.5* (13.1, 43.8)	2004-2010	13.3* (9.5, 17.3)	2010-2012	115.5* (75.6, 164.5)	-	-
Poland	2005-2014	5.4 (-6.6, 18.8)	2005-2012	19.4* (10.1, 29.4)	2012-2014	-47.6* (-71.3, -4.3)	-	-
Portugal	2000-2014	-0.6 (-1.9, 0.9)	-	-	-	-	-	-
Slovakia	2000-2014	5.2* (0.8, 9.7)	2000-2004	37.2* (21.1, 55.4)	2004-2008	-13.1 (-28.7, 5.9)	2008-2014	9.6* (1.9, 17.8)
Slovenia	2004-2014	8.9* (6.1, 11.8)	2004-2006	28.4* (2.4, 60.9)	2006-2014	6.4* (3.8, 9.0)	-	-
Spain	2000-2014	17.1* (9.4, 25.3)	2000-2005	57.6* (26.8, 95.9)	2005-2014	2.9 (-5.9, 12.5)	-	-
United Kingdom	2000-2014	-2.4* (-3.2, -1.7)	-	-	-	-	-	-

Abbreviations: APC: annual percent change; CI: confidence interval. *p-value<0.05 for change in trend.

Table 2. Joinpoint analysis for Alzheimer's disease hospital morbidity trends in men in the European Union, 2000-2014.

	Total study period		Period 1		Period 2		Period 3	
	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)
European Union	2000-2014	-0.5 (-1.8, 0.8)	2000-2004	6.4* (2.1, 10.9)	2004-2012	-1.4 (-3.2, 0.3)	2012-2014	-10.2 (-21.3, 2.4)
Austria	2000-2014	-1.7 (-7.4, 4.2)	2000-2002	92.8* (55.7, 138.7)	2002-2009	-1.5 (-5.0, 2.2)	2009-2014	-16.6* (-20.5, -12.6)
Belgium	2000-2013	9.4* (7.0, 11.9)	-	-	-	-	-	-
Croatia	2002-2014	-1.9 (-6.0, 2.4)	-	-	-	-	-	-
Cyprus	2005-2013	1.8 (-14.2, 20.9)	-	-	-	-	-	-
Czech Republic	2000-2014	4.3* (3.3, 5.4)	2000-2004	5.4* (0.3, 10.7)	2004-2007	-1.9 (-16.1, 14.6)	2007-2014	7.6* (5.4, 9.9)
Denmark	2000-2014	-3.4 (-7.1, 0.5)	2000-2009	4.6* (0.2, 9.3)	2009-2014	-19.6* (-27.7, -10.6)	-	-
Finland	2001-2014	2.8* (1.4, 4.2)	2001-2006	8.7* (5.2, 12.2)	2006-2014	-0.1 (-1.7, 1.5)	-	-
France	2000-2014	-6.8* (-9.7, -3.8)	2000-2007	2.7 (-1.8, 7.5)	2007-2014	-15.4* (-19.2, -11.5)	-	-
Germany	2000-2014	3.4* (1.8, 5.1)	2000-2003	17.3* (11.1, 23.8)	2003-2007	3.2 (-2.2, 9.0)	2007-2014	0.1 (-1.3, 1.6)
Hungary	2004-2014	2.1 (-2.7, 7.1)	-	-	-	-	-	-
Ireland	2000-2014	-2.5 (-4.9, 0.0)	-	-	-	-	-	-
Italy	2001-2014	-4.8* (-6.5, -2.9)	2001-2008	0.3 (-0.9, 1.6)	2008-2014	-10.7* (-12.1, -9.3)	-	-
Latvia	2004-2014	18.8* (3.7, 36.1)	-	-	-	-	-	-
Lithuania	2001-2014	8.4* (6.1, 10.8)	-	-	-	-	-	-
Luxembourg	2002-2012	-4.7 (-9.8, 0.6)	-	-	-	-	-	-
Netherlands	2004-2012	30.7* (14.3, 49.6)	2004-2010	15.3* (2.6, 29.7)	2010-2012	128.6* (14.1, 357.9)	-	-
Poland	2005-2014	5.5 (-6.4, 18.8)	2005-2012	19.4* (11.2, 28.2)	2012-2014	-47.4* (-69.1, -10.5)	-	-
Portugal	2000-2014	-1.3 (-3.2, 0.7)	-	-	-	-	-	-
Slovakia	2000-2014	6.2* (1.2, 11.4)	2000-2004	41.8* (18.4, 69.8)	2004-2009	-10.8 (-25.5, 6.8)	2009-2014	14.2 (-0.3, 30.9)
Slovenia	2004-2014	4.8* (1.9, 7.8)	-	-	-	-	-	-
Spain	2000-2014	17.8* (10.3, 25.8)	2000-2005	58.9* (31.1, 92.7)	2005-2014	3.4 (-4.4, 11.8)	-	-
United Kingdom	2000-2014	-1.9* (-2.7, -1.1)	-	-	-	-	-	-

Abbreviations: APC: annual percent change; CI: confidence interval. *p-value<0.05 for change in trend.

Table 3. Joinpoint analysis for Alzheimer's disease hospital morbidity trends in women in the European Union, 2000-2014.

	Total study period		Period 1		Period 2		Period 3	
	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)
European Union	2000-2014	-1.0 (-2.4, 0.5)	2000-2004	6.7* (2.2, 11.5)	2004-2012	-2.0* (-3.8, -0.2)	2012-2014	-11.8 (-23.1, 1.1)
Austria	2000-2014	-1.2 (-6.6, 4.4)	2000-2002	100.3* (14.8, 249.3)	2002-2014	-6.5* (-9.5, -3.3)	-	-
Belgium	2000-2013	10.8* (8.3, 13.3)	-	-	-	-	-	-
Croatia	2002-2014	-5.6* (-8.4, -2.7)	2002-2012	-8.1* (-11.1, -5.0)	2012-2014	22.3 (-20.2, 87.5)	-	-
Cyprus	2005-2013	14.3 (-0.6, 31.3)	-	-	-	-	-	-
Czech Republic	2000-2014	4.5* (3.8, 5.2)	-	-	-	-	-	-
Denmark	2000-2014	-1.3 (-4.1, 1.6)	2000-2012	1.4 (-1.5, 4.2)	2012-2014	-29.9 (-56.4, 12.8)	-	-
Finland	2001-2014	2.7* (1.4, 4.0)	2001-2007	7.0* (5.1, 8.9)	2007-2014	-0.7 (-2.1, 0.7)	-	-
France	2000-2014	-7.1* (-10.5, -3.7)	2000-2007	3.7 (-1.7, 9.4)	2007-2014	-16.8* (-21.2, -12.3)	-	-
Germany	2000-2014	3.0* (1.4, 4.6)	2000-2003	16.9* (11.2, 22.8)	2003-2008	2.3 (-0.8, 5.6)	2008-2014	-0.7 (-2.3, 1.0)
Hungary	2004-2014	-1.3 (-5.8, 3.5)	2004-2008	-14.0 (-26.1, 0.1)	2008-2014	6.8 (-1.5, 15.9)	-	-
Ireland	2000-2014	-3.6* (-5.2, -2.0)	-	-	-	-	-	-
Italy	2001-2014	-5.0* (-6.9, -3.2)	2001-2005	1.0 (-1.2, 3.3)	2005-2009	-2.3 (-5.7, 1.2)	2009-2014	-12.2* (-13.6, -10.8)
Latvia	2004-2014	21.6* (3.9, 42.3)	-	-	-	-	-	-
Lithuania	2001-2014	10.6* (7.1, 14.1)	2001-2004	34.5* (17.7, 53.8)	2004-2014	6.7* (4.5, 9.0)	-	-
Luxembourg	2002-2012	-6.0* (-8.5, -3.5)	-	-	-	-	-	-
Netherlands	2004-2012	26.1* (12.3, 41.7)	2004-2010	12.4* (6.1, 19.0)	2010-2012	111.0* (50.6, 195.6)	-	-
Poland	2005-2014	5.3 (-6.7, 18.9)	2005-2012	19.4* (9.6, 30.0)	2012-2014	-47.7* (-72.3, -0.9)	-	-
Portugal	2000-2014	0.1 (-1.6, 1.9)	-	-	-	-	-	-
Slovakia	2000-2014	4.8* (0.4, 9.4)	2000-2004	35.0* (18.6, 53.7)	2004-2007	-16.5 (-44.5, 25.8)	2007-2014	6.9* (0.7, 13.5)
Slovenia	2004-2014	11.5* (7.3, 15.9)	2004-2006	44.0* (14.0, 81.9)	2006-2014	7.4* (4.7, 10.2)	-	-
Spain	2000-2014	17.0* (9.1, 25.5)	2000-2002	-6.1 (-29.8, 25.7)	2002-2005	99.8* (49.3, 167.4)	2005-2014	0.1 (-2.5, 2.8)
United Kingdom	2000-2014	-2.9* (-3.7, -2.0)	-	-	-	-	-	-

Abbreviations: APC: annual percent change; CI: confidence interval. *p-value<0.05 for change in trend.

Figure 1. Trends in hospital morbidity from Alzheimer's disease in the entire European Union, 2000-2014.

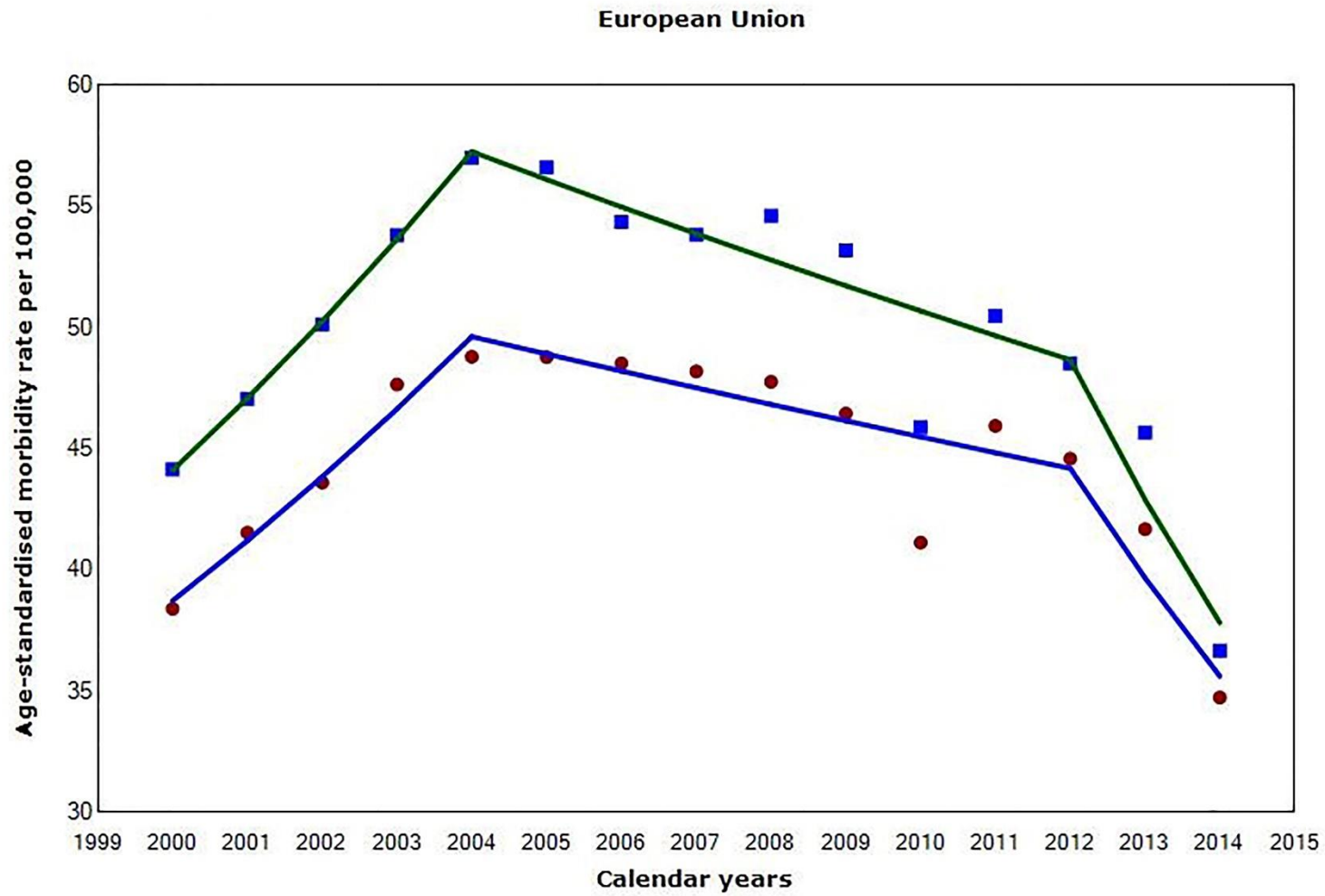


Figure 2. Trends in hospital morbidity from Alzheimer's disease in the member countries of the European Union, 2000-2014.

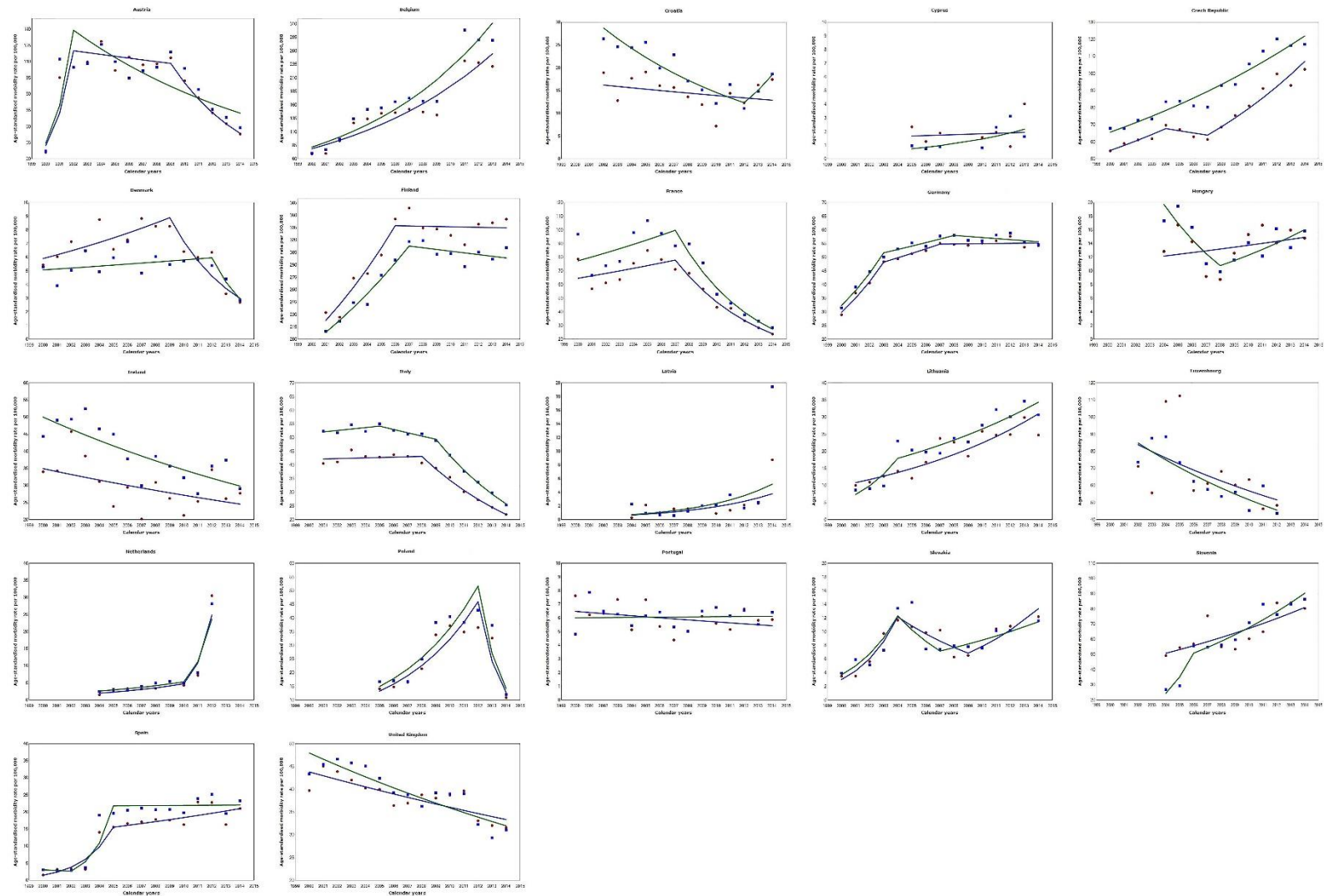


Figure legends

Square (blue): women (age-standardised morbidity rates)

Circle (red): men (age-standardised morbidity rates)

Green line: trends in hospital morbidity from Alzheimer's disease for European women.

Blue line: trends in hospital morbidity from Alzheimer's disease for European men.

Supplemental Data 1. Overall age-standardised hospital morbidity rates in the European Union, 2000-2014.

Countries	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
European Union	42.12	44.94	47.65	51.41	53.88	53.68	52.12	51.68	52.02	50.68	44.10	48.74	46.99	44.03	35.88
Austria	26.92	106.06	104.32	108.26	126.62	106.75	100.76	103.80	106.02	117.81	99.51	81.09	64.55	56.18	46.74
Belgium	69.36	74.35	94.63	131.24	143.95	149.61	158.09	164.24	158.26	156.74	-	277.10	264.08	260.03	-
Croatia	-	-	23.54	20.89	21.78	23.27	18.52	21.26	15.80	14.21	9.99	15.81	11.76	15.16	18.40
Cyprus	-	-	-	-	-	1.62	0.92	1.36	-	-	1.10	2.15	2.15	2.71	-
Czech Republic	63.36	64.76	68.47	69.54	78.45	77.97	74.45	73.51	84.16	87.15	96.84	105.11	112.37	108.19	111.83
Denmark	5.17	4.67	5.90	6.53	6.33	6.32	7.20	6.35	6.71	6.48	6.07	5.94	5.84	3.96	2.81
Finland	-	217.28	224.19	253.31	253.93	284.25	311.46	329.72	324.01	312.57	311.14	295.52	316.75	311.46	320.76
France	90.42	62.98	69.12	71.86	89.21	98.73	90.16	81.67	81.67	68.75	49.45	45.14	36.22	31.35	26.71
Germany	30.67	38.42	43.25	49.34	51.82	53.86	53.61	56.83	56.88	55.62	55.53	57.22	58.21	54.56	54.22
Hungary	-	-	-	-	15.60	18.45	15.50	10.42	9.45	11.93	14.57	13.46	15.28	14.15	15.47
Ireland	41.00	43.38	47.47	46.54	40.38	36.45	34.48	25.66	34.88	31.52	27.48	26.48	34.60	32.28	28.31
Italy	-	47.74	47.58	51.10	48.72	50.29	49.11	47.95	47.19	44.92	40.30	34.60	31.12	27.66	23.98
Latvia	-	-	-	-	1.72	1.38	0.74	0.97	1.48	2.11	1.82	2.99	1.97	2.37	16.43
Lithuania	-	9.23	9.47	10.51	20.30	18.01	18.69	20.66	23.41	21.31	26.82	30.26	28.30	32.83	28.64
Luxembourg	-	-	74.54	75.26	93.54	85.80	59.68	56.82	56.75	57.22	50.28	54.08	44.19	41.02	52.58
Netherlands	-	-	-	-	2.09	2.86	3.14	3.80	4.37	5.51	4.71	7.53	28.81	-	-
Poland	-	-	-	-	-	15.89	16.25	16.65	23.65	37.00	39.22	37.38	40.62	35.76	11.64
Portugal	5.83	7.25	6.47	6.65	5.30	6.54	6.06	4.92	5.05	6.23	6.28	5.72	6.54	5.58	6.12
Slovakia	3.79	4.95	5.40	8.11	13.10	13.05	8.13	8.27	7.34	7.20	7.71	10.23	10.21	-	11.85
Slovenia	-	-	-	-	33.77	36.23	55.58	59.91	56.99	56.52	67.59	76.42	77.65	82.09	82.91
Spain	2.58	2.98	3.15	3.56	17.37	18.27	19.21	19.83	19.73	19.71	18.66	23.60	24.36	18.33	22.43
United Kingdom	41.90	45.12	45.55	44.05	43.04	41.26	37.80	37.97	37.16	38.69	39.00	39.29	32.72	30.47	31.40

Supplemental Data 2. Age-standardised hospital morbidity rates in men in the European Union, 2000-2014.

Countries	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
European Union	38.40	41.54	43.60	47.65	48.79	48.78	48.52	48.19	47.76	46.45	41.13	45.94	44.59	41.68	34.74
Austria	26.14	95.38	104.67	109.74	128.77	101.93	114.23	107.13	108.05	113.57	92.34	76.70	62.65	52.56	43.04
Belgium	69.33	70.20	93.78	126.74	134.18	144.67	145.81	152.01	146.84	141.27	-	241.72	238.21	231.42	-
Croatia	-	-	18.92	12.81	17.70	19.07	16.09	15.67	13.63	11.95	7.23	14.41	12.32	16.22	17.44
Cyprus	-	-	-	-	-	2.35	1.28	1.89	-	-	1.58	1.96	0.91	4.03	-
Czech Republic	54.73	59.01	61.16	61.87	69.72	67.22	62.94	61.46	68.68	75.47	81.04	91.25	99.78	93.05	102.45
Denmark	5.45	6.04	7.14	6.45	8.76	6.59	7.28	8.84	8.27	8.27	6.42	6.00	6.37	3.33	2.71
Finland	-	232.41	226.82	274.06	279.60	302.03	345.55	358.98	334.80	333.53	325.84	314.47	339.34	341.02	345.39
France	78.66	56.95	61.39	63.69	75.69	85.01	78.41	71.20	68.40	56.91	43.48	42.75	33.53	28.46	23.84
Germany	28.99	36.98	40.54	48.38	49.42	51.32	52.42	55.12	54.69	54.38	55.16	56.05	57.65	53.71	54.29
Hungary	-	-	-	-	12.86	16.74	14.29	9.20	8.77	12.61	15.33	16.70	14.10	15.99	14.82
Ireland	34.03	34.29	45.77	38.63	31.16	23.90	29.49	20.22	30.91	26.24	21.29	25.35	34.63	26.15	27.76
Italy	-	40.60	41.12	45.50	43.12	42.89	43.79	43.15	40.75	38.90	35.56	30.21	27.25	24.51	21.94
Latvia	-	-	-	-	0.28	2.15	1.04	1.58	1.62	2.03	0.91	1.38	2.13	2.38	8.76
Lithuania	-	10.03	11.00	12.75	14.21	12.12	16.84	23.79	22.70	18.60	25.87	24.76	24.91	29.91	24.79
Luxembourg	-	-	71.20	55.68	109.26	112.44	57.04	61.18	68.27	60.30	63.50	46.42	48.43	-	-
Netherlands	-	-	-	-	1.53	2.55	3.36	3.27	3.45	5.36	4.30	7.22	30.55	-	-
Poland	-	-	-	-	-	14.11	14.79	16.54	21.46	33.87	37.23	34.90	36.54	32.71	10.92
Portugal	7.63	6.23	6.33	7.36	5.14	7.34	5.39	4.39	5.06	6.12	5.61	5.16	6.67	5.83	5.89
Slovakia	3.49	3.52	5.62	9.74	11.68	10.72	9.87	10.23	6.30	6.52	7.77	10.41	10.81	-	12.20
Slovenia	-	-	-	-	49.29	54.58	57.03	75.45	55.03	53.52	60.36	64.99	83.98	83.99	80.34
Spain	1.59	3.25	3.41	3.26	14.10	15.59	16.65	17.15	17.83	17.65	16.33	22.93	22.82	16.35	21.04
United Kingdom	39.72	45.08	43.90	42.04	40.27	39.99	36.44	36.97	38.79	38.07	38.73	39.66	33.09	32.05	31.58

Supplemental Data 3. Age-standardised hospital morbidity rates in women in the European Union, 2000-2014.

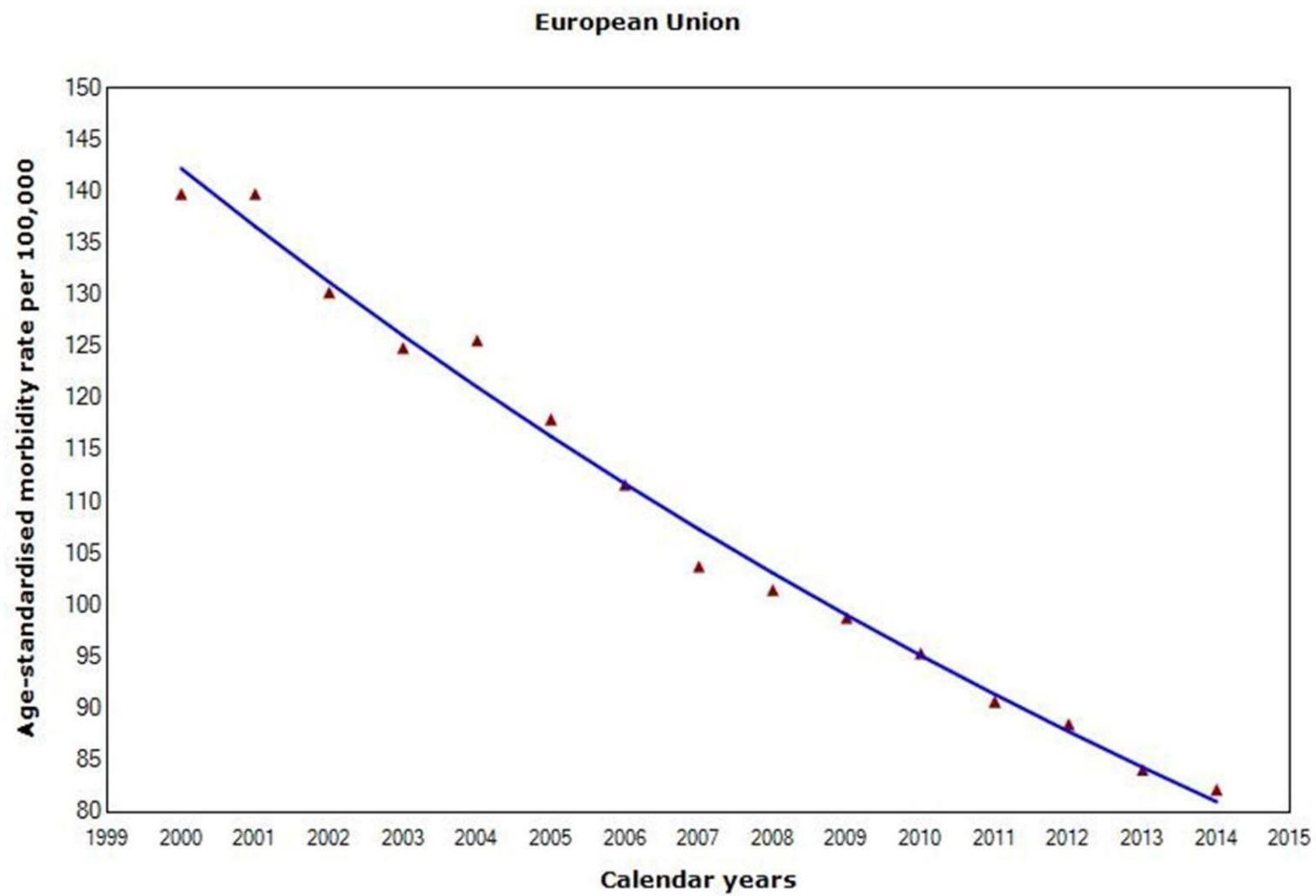
Countries	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
European Union	44.15	47.06	50.12	53.81	57.01	56.61	54.35	53.83	54.61	53.19	45.88	50.48	48.51	45.66	36.66
Austria	27.27	112.43	104.79	108.37	126.09	110.01	94.95	101.74	104.96	118.94	103.86	84.36	65.90	58.56	48.85
Belgium	70.58	77.15	96.78	134.62	151.74	154.67	165.90	172.66	166.92	166.72	-	298.69	280.36	279.62	-
Croatia	-	-	26.38	24.64	24.41	25.62	19.92	22.88	17.15	15.15	12.21	16.34	11.10	14.83	18.64
Cyprus	-	-	-	-	-	0.97	0.75	0.89	-	-	0.82	2.32	3.13	1.64	-
Czech Republic	67.95	67.76	72.55	73.44	83.50	83.81	81.04	80.34	93.01	93.65	105.61	113.11	120.19	116.33	117.12
Denmark	5.29	3.92	5.05	6.48	4.94	5.98	7.15	4.85	6.05	5.47	5.72	5.83	5.40	4.41	2.86
Finland	-	209.89	222.02	244.40	242.31	277.56	295.92	318.39	319.48	302.90	303.74	287.95	305.43	297.06	310.89
France	96.92	66.88	73.93	77.08	98.09	106.92	97.54	88.38	89.84	75.95	52.94	46.35	37.87	33.33	28.57
Germany	31.52	39.13	44.76	50.13	53.09	55.29	54.04	57.78	58.05	56.22	56.05	58.18	58.86	55.51	54.62
Hungary	-	-	-	-	17.32	19.46	16.41	11.04	9.88	11.62	14.11	12.19	16.17	13.44	15.87
Ireland	44.35	49.14	49.42	52.44	46.60	45.00	37.78	29.93	38.57	35.68	32.29	27.61	35.67	37.46	29.06
Italy	-	52.36	51.79	54.69	52.29	55.05	52.72	51.26	51.40	48.99	43.58	37.71	33.69	29.86	25.37
Latvia	-	-	-	-	2.28	0.98	0.68	0.60	1.24	2.06	2.19	3.64	1.71	2.57	19.44
Lithuania	-	8.66	9.09	9.87	23.04	20.35	19.81	19.45	23.88	22.77	27.66	32.22	30.12	34.69	30.72
Luxembourg	-	-	73.70	87.70	88.58	73.44	62.43	57.70	53.69	56.17	45.34	59.79	43.75	-	-
Netherlands	-	-	-	-	2.50	3.08	2.93	4.03	4.97	5.53	5.00	7.98	28.15	-	-
Poland	-	-	-	-	-	16.71	17.07	16.74	24.94	38.38	40.53	38.42	42.86	37.36	12.05
Portugal	4.82	7.88	6.50	6.29	5.44	6.17	6.44	5.34	5.02	6.50	6.77	6.16	6.55	5.54	6.43
Slovakia	3.95	5.93	5.14	7.29	13.43	14.29	7.47	7.42	7.93	7.80	7.59	10.13	10.19	-	11.62
Slovenia	-	-	-	-	26.87	29.46	55.66	54.89	56.23	59.74	70.93	83.15	76.28	83.11	86.34
Spain	3.13	2.86	2.92	3.80	19.10	19.67	20.55	21.19	20.67	20.80	19.78	23.97	25.19	19.58	23.33
United Kingdom	43.37	45.49	46.64	45.80	45.11	42.42	39.25	38.81	36.26	39.23	38.99	39.04	32.29	29.37	31.09

Supplemental Data 4. Joinpoint analysis for dementia hospital morbidity trends in the European Union, 2000-2014.

	Total study period		Period 1		Period 2		Period 3	
	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)	Years	APC ^a (95% CI ^b)
European Union	2000-2014	-3.9* (-4.2, -3.7)	-	-	-	-	-	-
Austria	2000-2014	-1.7* (-3.3, -0.1)	2000-2002	-19.9 (-36.3, 0.8)	2002-2014	-0.2 (-1.5, 1.2)	-	-
Belgium	2000-2013	-8.3* (-10.4, -6.3)	2000-2004	-5.3* (-7.5, -2.9)	2004-2007	-19.8* (-25.7, -13.4)	2007-2013	-1.3 (-2.5, 0.0)
Croatia	2002-2014	-0.1 (-1.1, 0.8)	-	-	-	-	-	-
Cyprus	2005-2013	89.0* (6.1, 236.5)	-	-	-	-	-	-
Czech Republic	2000-2014	-1.4* (-2.0, -0.8)	2000-2011	-0.7* (-1.4, -0.1)	2011-2014	-5.7* (-10.2, -1.0)	-	-
Denmark	2000-2014	-4.8* (-6.5, -3.2)	2000-2002	19.8* (0.4, 43.0)	2002-2014	-6.5* (-7.5, -5.5)	-	-
Finland	2001-2014	-4.2* (-4.5, -3.8)	-	-	-	-	-	-
France	2000-2014	-0.7 (-1.7, 0.2)	2000-2008	1.8* (1.0, 2.6)	2008-2014	-4.4* (-5.6, -3.2)	-	-
Germany	2000-2014	-7.1* (-7.5, -6.6)	2000-2007	-8.2* (-9.3, -7.1)	2007-2014	-5.9* (-7.0, -4.7)	-	-
Hungary	2004-2014	-4.3* (-5.6, -3.1)	-	-	-	-	-	-
Ireland	2000-2014	2.9* (0.7, 5.0)	-	-	-	-	-	-
Italy	2001-2014	-7.4* (-7.9, -6.9)	2001-2004	-11.1* (-13.6, -8.6)	2004-2014	-6.7* (-7.1, -6.3)	-	-
Latvia	2004-2014	4.9* (2.0, 7.8)	-	-	-	-	-	-
Lithuania	2001-2014	-9.2* (-11.3, -7.0)	-	-	-	-	-	-
Luxembourg	2002-2014	-2.2* (-3.2, -1.1)	-	-	-	-	-	-
Netherlands	2004-2012	-4.3* (-7.2, -1.3)	2004-2010	-1.1 (-3.4, 1.2)	2010-2012	-17.4* (-28.0, -5.3)	-	-
Poland	2005-2014	-0.9 (-2.3, 0.6)	-	-	-	-	-	-
Portugal	2000-2014	-3.6* (-5.0, -2.2)	2000-2003	-7.7* (-14.3, -0.6)	2003-2008	2.4 (-2.2, 7.4)	2008-2014	-8.9* (-11.1, -6.6)
Slovakia	2000-2014	-0.3 (-1.0, 0.4)	-	-	-	-	-	-
Slovenia	2004-2014	0.7 (-1.1, 2.6)	2004-2006	12.9 (-8.3, 38.9)	2006-2014	-0.9 (-3.1, 1.4)	-	-
Spain	2000-2014	-4.2* (-4.9, -3.5)	-	-	-	-	-	-
United Kingdom	2000-2014	-4.8* (-5.6, -4.0)	2000-2004	-2.4 (-5.3, 0.6)	2004-2007	-11.2* (-19.2, -2.4)	2007-2014	-2.0* (-3.3, -0.8)

Abbreviations: APC: annual percent change; CI: confidence interval. *p-value<0.05 for change in trend.

Supplemental Data 5. Trends in hospital morbidity from dementia in the entire European Union, 2000-2014.



Supplemental Data 6. Trends in hospital morbidity from dementia in the member countries of the European Union, 2000-2014.

